REMARKS

STATUS OF THE APPLICATION

Claims 1-17 were filed. Claims 4-8 and 10-17 have been withdrawn by the Examiner as being drawn to nonelected inventions or species (subject to being reinstated if Claim 1 is allowed).[1] Claims 1-3 and 9 stand rejected. Claims 18 and 19 have been hereby added.

For clarity, the Examiner's rejections are set forth below:

(1) Claims 1-3 and 9 are rejected under 35 U.S.C. § 112, first paragraph as not enabled.

(2) Claims 1-3 and 9 are rejected under 35 U.S.C. § 112, first and second paragraphs, as indefinite.

(3) Claims 1-3 and 9 are rejected under 35 U.S.C. § 103 as being obvious.

Applicants believe that the following remarks traverse the Examiner's rejection of the claims. These remarks are presented in the same order as they appear above.

(1) The Claims Are Enabled

Claims 1-3 and 9 are stand rejected under 35 U.S.C. § 112, first paragraph. The Examiner argues that the specification does not "enable one skilled in the art ... to make and/or use the invention" (Office Action, page 2). The Examiner asserts that "[t]he state of the art is such that is unpredictable from the mouse data disclosed in the specification as to how the instant invention could be used or the treatment of disease *in vivo* in humans" (Office Action, page 2). Specifically, the Examiner expresses the belief that "(1) the protein may be inactivated before producing an effect ... (2) the protein may not reach the target area ... and (3) other junctional properties ... may make the protein unsuitable for *in vivo* therapeutic use, i.e. such as adverse side effects..." (Office Action, pages 2-3). Applicants disagree. First, the animal model is an autoimmune model having nothing to do with cancer and the purported

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[1] While it is true that "election was made without traverse" (Office Action, page 2), this election was made with the proviso that "[i]n the event that a generic claim within Group I is not granted, for business reasons and without prejudice to the prosecution of generic claims and claims to other species, applicants elect the myelin protein species in Group I as embodied in Claim 3" (Applicants Response to Restriction Requirement, dated November 13, 1996). This was in direct response to the Examiner's statement that "[a]pplicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution ... if no generic claim is *finally* held to be allowable" (emphasis supplied, Office Action dated September 13, 1996, pages 2-3).

problems with animal models in cancer discussed by Osband *et al.* Second, the Examiner's concerns regarding proteolysis and half-life have no relevancy to the field of immunizations and vaccinations. These two issues are discussed more fully below.

A. The Animal Model Is An Autoimmune Model

In making the rejection, the Examiner first questions the animal models presented in the specification. It must be stressed that the Examiner has the initial burden to provide a **reasonable** basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557 (Fed. Cir. 1993); Manual of Patent Examining Procedure (MPEP) § 2164.03. In this case, however, the Examiner provides no **reasonable** basis for questioning the scope of enablement of the claimed invention.

The Examiner cites the Osband reference for the proposition that "animal models are not generally predictive of therapeutic efficacy in humans as relates to immunotherapy regimens." (Office Action, page 2). It is respectfully submitted that the Osband reference teaches no such thing. Even a cursory reading of the Osband reference reveals that the teachings of the reference are strictly in the context of *cancer* therapy. The very title indicates this context, namely "Problems in the investigational study and clinical use of *cancer* immunotherapy."

Osband notes that the problems with animal models in cancer stem from "the unique nature of the host-tumor relationship." (see page 193, right hand column). Osband argues that "owing to the extreme complexity of the host-tumor immunorelationship, animal models do no fully mimic the biology of human patients with cancer." (see last full sentence on page 193).

Without taking issue with Osband's point of view,[2] the "host-tumor relationship" has no relevancy to the therapy of autoimmune disease. Since the source of the problem (according to Osband) for animal models has no bearing to the present invention, the Examiner cannot reasonably reject the autoimmune animal model used in the present invention.

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[2] Of course, the FDA demands animal studies as a prelude to human cancer drug trials. Thus, Osband's point of view is not shared universally.

Moreover, there is no requirement under Patent Law for any data of any kind, let alone human data. *See Ex parte Nardi and Simier*, 229 U.S.P.Q. 79, 80 (Bd. Pat. App. & Int'f. 1986) ("[i]t is well established that examples are not necessary . . . "). In the present application, the specification provides clear examples of the claimed method working in an animal model. Most importantly, the results shown in the specification for the animal model do not provide any basis for believing that the same method would not work in other animals, including humans.

Finally, applicants submit that the enablement requirement of 35 U.S.C. § 112 "is different from the utility requirement of 35 U.S.C. § 101" (MPEP § 2164.07). In this regard, it is applicants' understanding that, on the orders of the Commissioner of the U.S. Patent and Trademark Office, the Examiner is not permitted to "backdoor" a 35 U.S.C. § 101 utility rejection by arguing that a specific utility of the claims is not enabled:

> If the applicant has not asserted any credible utility for the claimed invention or a utility would not be readily apparent to one of ordinary skill in the art, *reject the claims under section 101.*

60 Federal Register 97, 98 (1995), (emphasis supplied). Since applicants have asserted a credible utility that is backed up with experimental evidence, the Examiner has neither a basis for a 101 rejection, nor a 112 rejection. *See In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995).

B. Proteolysis And Half-Life Are Not Relevant

The present invention is in the field of immunizations and vaccinations. The administration of antigen is carried out on humans every day, including children. The issues of proteolysis and half-life are not relevant to such administrations. Specifically, there is no concern regarding antigen "reaching the target area" (Office Action, page 3). There are no "functional properties" (Office Action, page 3) for antigen. Indeed, antigen need not even be intact. As stated many years ago:

> "The sites of chemical activity which bring antibody and antigen together into combination, however, represent relatively small portions of these complex molecules. A single site may be thought of as equivalent to the region occupied by *three to five of the several hundred amino-acid units* in an average protein."

M. Burnet, "The Mechanism of Immunity" *Scientific American* (1961) (emphasis added).

Finally, the Examiner appears not to have considered the nature of one skilled in the art in the field of immunizations and vaccinations. Indeed, the rejection is unsupported by

any evidence of level of skill in the relevant field at the time the invention was made. Importantly, the Examiner is not free to substitute the subjective opinion of an Examiner for this necessary factual determination:

> "When patent examiners substitute their own opinion of the level of skill in the art for actual evidence, it results in the application of an inconsistent, subjective standard of patentability. . . . . Patentability should be independent of the examiner assigned to the application."

Amicus Curiae Brief of the Biotechnology Industry Association and the Bay Area Bioscience Center in the United States Court of Appeals for the Federal Circuit, Case No. 94-1202, In re Thomas F. Deuel, Yri-Sheng Li, Ned R. Siegel and Peter G. Milner. Without evidence that those skilled in the art would be unable to practice the instant invention, the Examiner's position is merely conclusory and cannot be maintained.

(2) The Claims Are Definite.

Claims 1-3 and 9 are rejected under 35 U.S.C. § 112, first and second paragraphs, as indefinite. Specifically, the Examiner asserts that "Claim 1 is indefinite in the recitation of 'Th2 Response Inducing Adjuvant' because it is unclear what this means or encompasses" and "[t]here is no disclosure in the specification ... or guidance as to how the identity of said compounds would be elucidated" (Office Action, page 3). Applicants disagree. The specification notes that such adjuvants are "defined functionally as those adjuvants which induce . . . a Th2 response upon administration." (See specification, page 3, line 22). Moreover, section III of the application (beginning on page 8) teaches how such Th immunity is to be screened and detected. Such a detailed teaching makes the claim term definite and enables a host of adjuvants.

Nevertheless, for business purposes and without acquiescing to the Examiner's rejection, the language objected to by the Examiner has been deleted and Incomplete Freund's Adjuvant has been specifically recited in Claims 1 and 18. Claim 9 has been cancelled. Applicants hereby expressly reserve the right to prosecute broader claims, including but not limited to the unamended claim, in the future.

Applicants assert that this amendment renders the Examiner's objection moot. Therefore, it is requested that this rejection be withdrawn.

(3) The Claims Are Nonobvious.

Claims 1-3 and 9 are rejected under 35 U.S.C. § 103 as being obvious in light of Namikawa *et al.* The Examiner argues that "Namikawa *et al.* teach that immunization with MBP in IFA ... prevents EAE in rats" and "[i]t would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed method because Namikawa *et al.* teach that immunization with MBP in IFA prevents EAE in rats and the art recognized similarities between EAE and human MS" (Office Action, page 4). Applicants cannot agree with the Examiner's characterization of the reference.

A. The Reference As A Whole Does Not Teach The Invention

The Namikawa reference teaches that BP in IFA is an encephalitogen, albeit "relatively weak" (see p. 932, first paragraph). "Histological examination of coded specimens also showed only minimal evidence of EAE after repeated immunization with BP in IFA." (see p. 932, right hand column, last sentence). These teachings do not suggest that someone with autoimmune symptoms should be treated with BP in IFA. Indeed, quite the opposite. These teachings suggest that BP in IFA will cause mild EAE symptoms.

Moreover, the protective effects against challenge with BP in CFA were not complete. The reference notes that "two of the nine rats pretreated with BP/IFA developed clinical signs of EAE after challenge." (p. 933, left-hand column, second sentence).

The Examiner is not free to ignore these teachings. "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992). See also *In re Fine*, 837 F.2d 1071, 1075, 5 USPQ2d 1596 (Fed. Cir. 1988).

The Examiner cannot point to anything in the reference that suggests that someone having disease should be immunized as set forth in Claim 1. Applicants strongly assert, therefore, that the Examiner is not permitted to maintain the rejection without citation to a prior art reference that teaches **all** of the elements of the claimed method:

> To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.

Manual of Patenting Examining Procedure (MPEP) § 2144.03. Furthermore, the Examiner is reminded that:

FACT THAT THE CLAIMED INVENTION IS WITHIN THE CAPABILITIES OF ONE OF ORDINARY SKILL IN THE ART IS NOT SUFFICIENT BY ITSELF TO ESTABLISH *PRIMA FACIE* OBVIOUSNESS

Emphasis in original, MPEP § 2143.01.

B. The Methods Of Claim 2 and 18 Are Not Taught

Claims 2 and 18 contain the further limitations that cytokines be detected from the cells of the subject immunized. The cited reference does not teach the measurement of cytokines, let alone the use of a hydrophobic membrane having a cytokine binding ligand.

The Examiner notes that "Namikawa *et al.* teach that after immunization, the response of cells to a T cell mitogen is tested" (Office Action, page 4). Applicants agrees that the **proliferative** response to a T cell mitogen is tested. However, no cytokines are measured.

Perhaps understanding the weakness of the cited reference as a basis for a 103 rejection, the Examiner argues that the claimed method is obvious because "ELISA assays are known in the art." (Office Action, page 4). It is respectfully submitted that this general assertion does not rise to the level of a 103 rejection. Specifically, while certain types of ELISA assays are known (particularly assays measuring antibodies), the claimed method is not known. Merely asserting that "ELISA assays are known" does not provide the showing that each and every element of Claims 2 and 18 can be found in the art. Consequently, the Examiner has not established a *prima facie* case of obviousness.[3] It is requested that this rejection be withdrawn.

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[3] This is not to say that the mere recitation of any reference will suffice. The Examiner also has the additional hurdle of showing why the references may be combined. As the Examiner undoubtably is aware, it is impermissible "simply to engage in a hindsight reconstruction of the claimed invention, using the Applicant's structure as a template and selecting elements from references to fill the gaps. The references themselves must provide some teaching whereby the Applicant's combination would have been obvious." *See Interconnect Planning Corp. v. Feil*, 227 U.S.P.Q. 543 (Fed. Cir. 1985).

CONCLUSION

For the reasons set forth above, it is respectfully submitted that Applicant's claims as amended should be passed to allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned collect at (415) 705-8410.

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Peter G. Carroll
Registration No. 32,837

MEDLEN & CARROLL, LLP
220 Montgomery Street, Suite 2200
San Francisco, California 94104
415/705-8410